

REMARKS

Applicant has concurrently filed a Request for Continued Examination and, therefore, respectfully requests consideration of the above amendments and the following remarks prior to further examination of the present application.

Claims 1-10, 12 and 13 are currently pending in this application. Claims 1 and 10 are amended. Claim 11 is cancelled. New claims 12 and 13 have been added. No new matter has been added.

Applicants' Response to Rejection under 35 U.S.C. §103 over Buch in view of Singer and Giorgetti

Claims 1-10 are rejected under 35 U.S.C. § 103(a), as allegedly being obvious over U.S. Patent No. 5,723,106 to Buch et al. (hereinafter "Buch") in view of U.S. Patent No. 5,294,433 to Singer et al. (hereinafter "Singer") and further in view of U.S. Patent No. 6,194,462 to Giorgetti (hereinafter "Giorgetti"). Applicants respectfully request reconsideration.

The Examiner contends that Buch discloses an oral composition including eucalyptol, menthol, methyl salicylate, thymol, benzoic acid, a sugar alcohol and a surfactant. According to the Examiner, Buch teaches the use of its composition for treating gingivitis. The Examiner further contends that Singer teaches the use of an anti-inflammatory agent for the treatment of gingivitis. According to the Examiner,

The teaching of Buch differs from the claimed invention in the incorporation of nonsteroidal anti-inflammatory drug (NSAID) . . . to said oral care composition To incorporate such teaching into the teaching of Buch, would have been obvious in view of Singer who teaches the use of the anti-inflammatory agent such as ketorolac, flurbiprofen, ibuprofen, naproxen, indomethacin, aspirin, ketoprofen, piroxicam for treating gingivitis, and further in view of Girogetti who demonstrates the art recognition in using anti-inflammatory agent in the treatment of gingivitis.

(Office Action, at Page 6).

Applicants have amended independent claims 1 and 10 herein to further define the invention. In particular, Applicants have added a recitation in claims 1 and 10 that requires the four essential oils, i.e., thymol, methyl salicylate, menthol and eucalyptol, to be “present in said composition in synergistically effective amounts.” None of the cited references disclose or suggest that this combination of oils is synergistically effective against inflammation.

As further support, Applicants submit herewith a declaration under 37 C.F.R. §1.132 executed by Pauline C. Pan, Ph.D. (hereinafter “Rule 132 declaration”).

The Rule 132 declaration shows that the combination of thymol, methyl salicylate, menthol and eucalyptol (hereinafter referred to as the “essential oils”) exhibited synergistic inhibitory activity against an enzyme associated with inflammation in the oral environment. (Rule 132 Declaration; ¶¶ 14-15). The combination of the four essential oils exhibited marked superiority over each of the essential oils individually. (Rule 132 Declaration; ¶ 15). Such synergistic anti-inflammatory activity by the combination of the four essential oils was unexpected. (Rule 132 Declaration; ¶¶ 10, 18).

The declaration describes an assay that was employed to measure the amount of inhibition of the mPGES-1 enzyme, which is associated with inflammation in the oral environment, by each of the test compounds. The compounds tested included each of the four essential oils individually, as well as the combination of the four essential oils. Additionally, several commonly known anti-microbial agents and antibiotics were tested. The results of the assay are shown in Table 1 of the declaration. The inhibitory activity for each test compound is represented by the IC₅₀ value, which is the concentration of the compound required for 50% inhibition of the enzyme. Accordingly, the lower the IC₅₀ value listed in Table 1, the greater the inhibitory activity of the compound.

As described in the declaration, the four essential oils individually showed hierarchical activity. (Rule 132 Declaration; ¶ 14). Thymol showed the greatest activity individually, with an IC_{50} of mPGES-1 inhibition of 0.05%. The combination of the four essential oils, however, exhibited synergistic activity. The IC_{50} for the combination of the four essential oils was 0.00412%. This level was markedly lower (more than 10 times) than any of the four essential oils individually. (Rule 132 Declaration; ¶ 15).

The declaration also explains that the residual level of the four essential oils expected to be found in the mouth following a typical single rinse with a mouthwash containing the oils is 0.025%. As mentioned above, the IC_{50} of the four essential oils demonstrated in this assay was 0.00412%. Therefore, the concentration of the four essential oils found to inhibit 50% of the enzyme tested in this assay was significantly below the residual level expected to be found in the mouth after a typical mouthwash rinse. As stated in the declaration, “[t]his indicates that a typical, single rinse with a mouthwash containing the four essential oils is enough to impart the anti-inflammatory properties thereof.” (Rule 132 Declaration; ¶ 16).

On the basis of these test results, Dr. Pan concludes that:

the inhibitory activity of the combination of the four essential oils against mPGES-1 in this experiment was unexpected. The results of this experiment suggest that the combination of the four essential oils may be useful in reducing PGE_2 levels in the oral environment, and thus, have anti-inflammatory properties.

(Rule 132 Declaration; ¶ 18).

In view of the showings in the Rule 132 declaration, the combination of the four essential oils, as recited in the present claims, exhibit synergistic anti-inflammatory effects. Such results were unexpected to a person of ordinary skill in the art. Buch, Singer and Giorgetti are wholly devoid of any teaching of anti-inflammatory properties of the four essential oils. Further, Buch, Singer and Giorgetti fail to teach or suggest the synergistic anti-inflammatory properties of the

combination of the four essential oils, which were unexpectedly demonstrated by the assay described in the declaration. In view thereof, there would be no suggestion for one of ordinary skill in the art to combine the four essential oils in synergistically effective amounts, as recited in the amended claims, with an NSAID to provide an oral composition that is effective against inflammation.

Therefore, Applicants respectfully submit that the obviousness rejection over Buch, Singer and Giorgetti has been overcome, and claims 1-10 are patentable over the cited combination.

It also is noted that Applicants have added new claims 12 and 13. Claim 12 is similar to independent claim 1 except that it requires the four essential oils to be "present in amounts effective against inflammation." In claim 13, which depends from claim 12, the NSAID is specified as acetaminophen. None of the cited references disclose or suggest that this combination of essential oils is effective against inflammation. Moreover, the unexpected results of the combination of essential oils described in the Rule 132 Declaration similarly are applicable to new claim 12. In view of such results, there would be no suggestion for one of ordinary skill in the art to combine the four essential oils in anti-inflammatory amounts, as recited in the amended claims, with an NSAID to provide an oral composition that is effective against inflammation. It is respectfully submitted that claims 12 and 13 provide an additional basis of patentability.

Applicants' Response to Rejection under 35 U.S.C. §103 over Buch in view of Singer, Giorgetti and Rajaiah

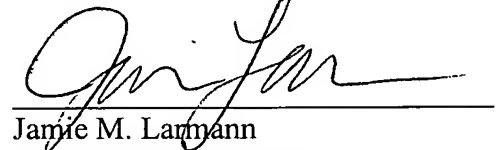
Claim 11 is rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Buch in view of Singer, Giorgetti and U.S. Patent No. 6,509,007 to Rajaiah et al. (hereinafter "Rajaiah"). Applicants have cancelled claim 11 herein, and thus, respectfully submit that this rejection has been overcome.

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The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R. § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number given below.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Jamie M. Larman", is written over a horizontal line.

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